SUBSTITUTED CYCLOHEXANONES FOR TERPENE SYNTHESES

BY

JAMES BEVERLEY McPHERSON, JR.

A.B., Kenyon College, 1941
M.S., University of Illinois, 1942

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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Introduction

Most of the monocyclic terpenes are regarded as derivatives of *p*-menthane. In most cases they contain a functional group and one or more olefinic bonds located at various points in the *p*-methane skeleton. Thus the isopropyl, isopropenyl, or isopropylidene group is encountered among these terpenes. Cylohexanone, properly substituted with one of these groups, should serve as an excellent source for the synthesis and complete proof of structure of certain of these terpenes. This report is concerned with methods for preparing such cylohexanones.

For example the synthesis of *dl*-phellandral has recently been effected using 4-isopropylcyclohexanone as one of the starting materials[1]. Perkin reported the preparation of 4-isopropenylcyclohexanone from which he synthesized β-terpineol[2]. He reported also the preparation of 4-isopropylidenecyclohexanone, but did not, as might be expected, use this as a source for the synthesis of γ-terpineol[3].

It was felt that other methods should be studied for the preparation of 4-isopropenylcyclohexanone and 4-isopropylidenecyclohexanone so that these compounds could be used as starting materials for the synthesis of terpenes such as perillaldehyde, β-terpineol, and γ-terpineol.

Discussion of Results

The method of Bruson[4] was followed in the preparation of γ-acetyl-γ-isopropenylpimelonitrile (I), γ-acetyl-γ-isopropenylpimelic acid (II), and γ-carboxy-γ-isopropenylpimelic acid (III).

The tricarboxylic acid (III), decarboxylated and ring closed at 285-320° in the presence of barium carbonate, gave a

mixture of 4-isopropylidenecyclohexanone (IV) and 4-isopropenylcyclohexanone. The structure of this ketone was proved by its treatment with ozone, which resulted in the formation of acetone, 1,4-cyclohexanedione, and small amounts of formaldehyde and formic acid.

The formation of 4-isopropylidenecyclohexanone (IV) showed that during the pyrolysis reaction the isopropenyl group rearranged to an isopropylidene group. Since the decarboxylation appeared to occur in two steps, it was necessary to determine at which step the rearrangement had occurred.

The tricarboxylic acid (III) was decarboxylated at 195-205° in the presence of copper-bronze resulting in the formation of 4-isopropylidenepimelic acid (V), the structure proof of which is mentioned below.

Treatment of the dinitrile (I) with sodium hypochlorite at 0-10° in aqueous dioxane as a solvent gave γ-carboxy-γ-isopropenylpimelonitrile (VI). This monocarboxylic acid was decarboxylated at 200-240° in the presence of copper-bronze, resulting in the formation of 4-isopropylidenepimelonitrile (VII). Since this dinitrile gave acetone, but not formaldehyde, when treated with ozone, the isopropylidene form was present but not the isopropenyl form. Hydrolysis of the dinitrile (VII) gave the dicarboxylic acid (V) which was shown to be identical with the acid obtained by the previous method. Thus it was shown that in the pyrolysis of the tricarboxylic acid (III) the decarboxylation must have occurred before the ring closure, and the rearrangement of the isopropenyl to isopropylidene group must have occurred during this decarboxylation.

During the decarboxylation of the dinitrile (VI), a solid by-product was obtained which was shown to be isomeric with the starting material. This by-product was proved to be α-cyanoethyl-α-isopropenylglutarimide by its hydrolysis to the symmetrical monoamide of the tricarboxylic acid (III). A mechanism for the formation of this by-product has been suggested involving the partial hydrolysis of one of the nitrile groups in the dinitrile (VI), followed by dehydration between the re-

sulting amide group and the carboxyl group.

Ring closure of the dinitrile (VII) by the Ziegler method gave 2-cyano-4-isopropylidenecyclohexanone, which was hydrolysed and decarboxylated to give 4-isopropylidenecyclohexanone (IV). The 2,4-dinitrophenylhydrazone of this compound was shown to be identical with the same derivative of this ketone when obtained by the previous method.

Treatment of the cyclic ketone (IV) with methylmagnesium iodide gave γ-terpineol; which constitutes a total synthesis of this terpene.

Infrared absorption spectra were studied for this series of compounds.

BIBLIOGRAPHY

1. Frank and Shotwell, "Abstract of Papers, A.C.S. Meeting," St. Louis, Mo., Sept., 1948, p. 60L

2. Perkin, J. Chem. Soc. 85, 670 (1904)

3. Perkin and Simonsen, *ibid.* 91, 1736 (1907)

4. Bruson and Riener, J. Am. Chem. Soc. 65, 18 (1943)

VITA

The author was born in Cleveland, Ohio, on May 9, 1920. He attended the public schools of Cuyahoga Falls, Ohio, and was graduated from high school in June, 1937. He received the Bachelor of Arts degree at Kenyon College in June, 1941. He entered the Graduate College of the University of Illinois in the autumn of the same year, and was granted the degree of Master of Science in Chemistry in August, 1942. He continued his graduate studies until the summer of 1943. For the academic year of 1943-1944 he was employed by the University of Illinois as a part-time teaching assistant and as a research chemist on the Synthetic Rubber Research Project. In June, 1944 he entered the Navy. He was released to inactive duty with the rank of Lt. (jg), U.S.N.R. in August, 1946, and returned to the University of Illinois to complete his work for the doctorate. During the course of his graduate studies he was employed as a part-time teaching assistant and held a University of Illinois Fellowship.

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